"DESIGN, DEVELOPMENT AND EVALUATION OF TOPICAL POLYHERBAL FORMULATIONS FOR BACTERIAL SKIN DISEASES"

A SYNOPSIS SUBMITTED FOR THE REGISTRATION OF *DEGREE OF*

DOCTOR OF PHILOSOPHY

In the Faculty of Pharmaceutical Sciences & Technology

Submitted

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Introduction:

Skin disorders represent the next most common extra intestinal complication of inflammatory bowel diseases affecting up to 20% of people. Previous studies on populations suggest that around 23-33% have a skin problem. Skin conditions are the most frequent reason for people to consult their general practitioner with a new problem. The quality of life of people with skin diseases such as psoriasis, atopic eczema, and acne can be significantly impaired andsuch impairments can be greater at times than for life threatening conditions such as cancers. Most common skin diseases are concerned with significant psychosocial-morbidity which may go unrecognized without the use of appropriate assessment tools. There were nearly 4,000 deaths due to skin disease in 2005 of which 1,817 were due to malignant melanoma.[(1)]Common skin disorders areeczema, psoriasis, generalized pruritus, urticaria, Acne, rosaceous, Bacterial, Viral, Fungal infections, disorders of hairs and nails, skin tumors, leg ulcers, leprosy, dermatitis, skin allergy, scabies and swellings etc. [(2)]

Skin is the largest organ of the body. The important functions of the skin are as follows:

- Provide a protective barrier against mechanical, thermal, physical injury and hazardous substances.
- Prevent loss of moisture.
- Reduce harmful effects of UV radiation.
- Act as a sensory organ.
- Help to regulate body temperature.
- Act as immune organ to detect infection.
- Production of Vitamin D.
- Protect our bodies from germs.
- Allow us to have the sense of touch.[(3,20)]

While performing all these function skin is affected by various diseases and disorders. The most damaging sequence of disruption to the skin is invasion by pathogenic microorganisms. Apart from these there are various allergic conditions which attack the skin. In people with skin disorders, the skin barrier does not work as well. The skin has less water retaining properties and moisture is easily lost from the skin causing it to dry out easily.

Lot of drugs is being tried for skin diseases, but few have indicated drug resistance, and few have serious side effects. The search for newer source of antibiotics is a global challenge for research institutions, pharmaceutical companies, and academics. Many allopathic drugs used are having side effects such as contact allergy, local irritation, scaling, photosensitivity itching and redness etc. to be costly, having side effects to humans. Also many drugs are toxic at certain concentration.

On the other hand the herbal drugs are safe from side effects as well as harmful effects. In order to prevent antibiotics resistance of pathogen there is need to discover the new compounds.Medicinal plants have a great potential to cure the different diseases but also as a potential material for maintaining good health. Ayurveda is a traditionalsystemof medicine. The philosophy behind the ayurveda is preventing unnecessary suffering and living a long healthy life.[1] Ayurveda involves the use of natural elements to eliminate the root cause of disease by restoring balance at the same time create a healthy life-style to prevent the recurrence of imbalance.[4]In ayurveda single o multiple herbs are used for the treatment. The ayurveda literature highlighted the concept of poly herbals to achieve a greater therapeutic effect. The active phytochemical constituents of individual plants are insufficient to achieve a desirable therapeutic effect and reduce the toxicity.[7]

Application of traditional herbal medicine is widespread in different regions of the world. Many people worldwide use various plant based products for treating skin problems.[8] These herbs are a rich source of active ingredients and can be safer and more cost effective for the treatment of different skin diseases.[5, 21]Literature survey reveals that plants have always been proven as a better source of drugs, when it comes to treatment of skin diseases. Hence, it is an emergence worth to undertake this study to design and develop the polyherbal formulation such as cream, lotion, ointment, gel, nanogel and nanoemulsion etc. for the treatment of Acne, Eczema, Psoriasis, Dermatitis, Warts, Sunburn, Impetigo, Pruritus, Urticaria, Skin allergy, Swellings and other infectious skin diseases. [9]

Objectives of the proposed project:

The broader objectives set for the studies are as follows-

- To formulate a novel topicalpolyherbal formulation for thetreatment of skin diseases, which is safe, well-tolerated, and non-toxic, with minimal and reversible adverse reactions or side effects?
- To minimize relapse or recurrence of the skin diseases following completion of a treatment regimen.
- To provide a novel polyherbal formulation, which is selective, simple, efficient and cost-effective?

Literature survey:

- **Smita Jain and u.k.patil (2011):** Formulated a polyherbal cream with wound healing activity. Formulation were designed by using ethanolic extract of *Argemone Mexicana, Cassia Tora, Evolvulus Alsinoids, Ocimum Centum, Curcumas Sativus* by phase inversion emulsification techniques. After evaluation the formulated herbal cream is most effective and safer usage in wound repair process.[10]
- **Y,m, charde et. al (2014):**Formulated and evaluated a herbal formulation for the treatment of acne. The present research work deals with formulation of herbal gel with ethanolic extracts of *Neem (leaves), Nutmeg (fruit) and Black pepper (fruit*) and evaluated for various physicochemical properties and antimicrobial activity. From evaluation it is concluded that this is an effective polyherbal formulation for the treatment of acne.[11]
- **Allah Nawas et. al(2014):** Formulated a topical polyherbal formulation Dermidoc cream consisting of natural ingredients that have been clinically proved for its anti-itching and anti-inflammatory activity and has been advocated to treat skin ailments especially dermatitis. Dermidoc cream consist of *Cleome brachycarpa, Calendula officinalis, Psoralen carylifolia and Rheum emodi wall.* From evaluation it is concluded that Dermidoc cream has shown efficacy in mild to moderate cases on applying locally to the affected parts.[12]
- **Kavitha A N et.al (2013):** Designed, formulated and evaluated a polyherbal ointment comprising of methanolic extract of the leaves of *Tectona grandis, Ficus religiosa, Caesalpinia* etc. This study revealed that the polyherbal ointment may be used as a potential herbal formulation for wound healing.[13]
- **Prakash Vaman Rao Diwan et al:** A patent on herbal formulation useful as therapeutic and cosmetic applications for the treatment of general skin disorders.[14]
- **Sudipta Das et.al:** Formulated and evaluated an herbal gel containing *Clerodendron infortunatum* leaves extract used for certain skin diseases, inflammation, burning sensation. This study reveals that natural remedies are more acceptable in the belief that they are safer with fewer side effects than the systemic ones. These herbal formulations have growing demand in the world market.[15]
- **Prasana A. Datar:** Formulated and evaluated polyherbal gel prepared using carbopol 934 for treating skin diseases in comparison with ointment using emulsifying ointment. This study deals with topical drug delivery system composed of polyherbal including *Neem, Tulsi, Aloe and fenugreek* which are having antifungal and antibacterial activity in the form of gel and were

evaluated for various physicochemical parameters like pH, viscosity, spreadability, skin irritations test and microbial evaluations. Such study reveals that gels are free from irritation and have better antimicrobial activity and this gel can be used for treating skin diseases.[16]

- **P.H. Rajasree et.al:** Formulated and evaluated antiseptic polyherbal ointment. The ointment were formulated using methanolic extract of *Azardirachta indica, chromolaena odorata, mimosa pudica, samadera indica* and evaluated for its physicochemical propertiey, antibacterial and antioxidant activity. Overall result of this study reveals that this is an effective polyherbal antiseptic oinmeant.[17]
- **Anand kumar et.al**: Developed a herbal formulations which has anti-inflammatory and immuomodulatory properties and is a chelating agent for various toxins in the blood. And has been advocated to treat various skin disorders such as chronic lichens planus, psoriasis, chronic lichen simplex, chronic eczema and various allergies lead to dermatitis.[18]
- **Arvind negi et**.al: evaluated a noble herbal gel formulation containing extract from the leaves *Eupaterium adenophorum* for its topical anti-inflammatory activity against carrageenan induced oedema. This study reveals that such gel possesses significant topical anti-inflammatory properties, supporting their traditional use for the treatment.[19]
- **Literature survey** reveals that many medicinal plants prove to be an excellent beauty product, helps to prevent wrinkles, blackheads, pimples, dryness, rashes. Also helps to attain hormonal balance in women. Medicinal plants have an ability to improve the tonicity of skin by cleansing the blood. As a diaphoretic it is able to bring a sweat and help to detox the body through the pores of skin and many plants skin smoothening, softness, skin whitening properties.[22,23]

Materials and methods of research:

Materials:

Drugs:*Melia Azadirachta, Ocimum Sanctum, Curcuma Longa, Argemone mexicana, sesamum indicum, Tectona grandis, Alove vera, Fenugreek and some other medicinal plants.*

Methods:

1. ***Collection and authentication of plant material***

   The plant will be collected, authenticated, cleaned, dried and powdered for further process.

2. ***Preliminary Phytochemical Investigation:***

   A. Extraction:

   The plant materials will be subjected for extraction with different solvents (Non-polar to Polar).

   B. Preliminary phytochemical investigation:

   Preliminary phytochemical investigation ofextract is carried out by qualitative chemical test and chromatographic technique.

3. ***Acute toxicity study***

   For the determination of safe dose of polyherbal formulation will be subjected for the acute toxicity according to OECD guidelines.

4. ***Formulation of topical polyherbal formulation.***

5. ***Evaluation for various physicochemical parameters.***

   - ❖ pH
   - ❖ Viscosity
   - ❖ Spreadability
   - ❖ Extrudability
   - ❖ Skin irritancy study
   - ❖ *In-vitro* diffusion study
   - ❖ Stability studies.

6. ***Pharmacological screening of polyherbal formulations.***

   The polyherbal formulations will be subjected for study of antibacterial and anti-inflammatory activity using screening model.

Plan of Work:

1. Literature survey
2. Selection of plants.
3. Collection of plant material
4. Authentication of plant material
5. Extraction
6. Preliminary phytochemical investigation of extract
7. Development of suitable topical polyherbal formulations- gel / cream.
8. Pharmacological screening
    a. Acute Toxicity Study.
    b. Evaluation of Anti-microbial activity.
    c. Evaluation of Anti-inflammatory activity

8. Data interpretation and thesis writing.

Tentative duration of work:

Sr. No.	Work to be Completed	Duration
1	Literature survey	8 Months
2	Collection and, Authentication of plant material.	2 Months
3	Extraction, Preliminary phytochemical screening of extract.	6 Months
4	Development of Topical polyherbal formulations.	6 Months
5	Physical evaluation of formulation.	2 months
6	Acute toxicity study.	2 Months
7	Pharmacological screening of formulation.	6 Months
8	Data interpretation and thesis writing.	4Months
Total Duration of Project36 Months		

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